achievement of steady state. The half life ($t_{1/2}$) of voriconazole was 5.09±5.15 hours. The dose normalized (per mg) AUC (mg*hr/ml) was 0.111±0.081. Voriconazole dose did not correlate with AUCo-∞ (r^2 = 0.028). There was a good correlation between AUCo-∞ and C_{trough} (r^2 = 0.94). Population estimates of bioavailability, clearance, apparent volume of the central compartment (Vc) and apparent volume of peripheral compartment (Vp) were 46.5%, 5.76L/hr, 19.4L and 58.8L.
Conclusions: The bioavailability of voriconazole was significantly lower in pediatric BMT patients than in non-transplant adult subjects. The $t_{1/2}$ at steady state tended to be lower than adult patients. Our study suggests that pediatric patients may require dosing higher than 7 mg/kg twice daily. The wide individual variability and the lack of correlation between dose and AUC support therapeutic monitoring of voriconazole and dose adjustments based on steady state blood levels.

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SAFETY AND EFFICACY OF INTRAVENOUS PENTAMIDINE IN CHILDREN AND ADOLESCENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Pneumocystis carnii pneumonia (PCP) is a potentially life-threatening but preventable infection that may occur after hematopoietic stem cell transplantation (HSCT). Although prophylaxis with trimethoprim-sulfamethoxazole has been shown to be effective in the prevention of PCP, the development of neutropenia limits its use in the early post-transplant period. Aerosolized pentamidine is a commonly used second line agent, but the need to have the drug administered via respiratory route may increase the risk of infection. Intravenous pentamidine has been used in the prevention of PCP in the post-transplant period, although there are few trials published in the literature evaluating its safety and efficacy. A recent series studying the use of intravenous pentamidine as secondary prophylaxis in children with cancer receiving conventional chemotherapy reported a breakthrough rate of 1.3%. We evaluated the overall efficacy of intravenous pentamidine, toxicity profile, and overall impact in the prevention of PCP in HSCT recipients.
Patients and Methods: Retrospective review of medical records of children who underwent HSCT from Jan 1, 2005 – October 1, 2011 who received intravenous pentamidine as first line PCP prophylaxis initiated at admission. Demographic, clinical, microbiologic, management, and outcome data was collected.
Results: 170 consecutive pediatric patients were given intravenous pentamidine before myeloablation and then every 28 days until the subject was 6 months post-HSCT, had stable neutrophil recovery (ANC >1000 without growth factor support), had discontinued immunosuppression and did not have evidence of chronic graft versus host disease.). No cases of PCP were seen in this cohort. Ten (6%) had a grade I side effect of nausea/vomiting requiring slower infusion time and 2 (1%) had a grade IV reaction with anaphylaxis and hypotension requiring transfer to the intensive care unit for management.
Conclusions: Our pediatric HSCT patients receiving pentamidine had no episodes of breakthrough PCP, and the incidence of side effects was low. Given the potential neutropenic effects of trimethoprim-sulfamethoxazole, compliance with drug administration, and inferior efficacy of other PCP prophylactic medications, intravenous pentamidine should be considered as first line therapy in the prevention of PCP in children undergoing HSCT.

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IDENTIFYING RELIGIOUS/SPIRITUAL (R/S) PERSPECTIVES OF ADOLESCENTS AND YOUNG ADULTS RECEIVING BLOOD AND MARROW TRANSPLANT: A QUALITATIVE STUDY

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Bone marrow transplant (BMT) or hematopoietic stem-cell transplantation (HSCT) are difficult treatments for life threatening illnesses; the emotional stress experienced by patients of any age is high. Religion/spirituality (R/S) is commonly used by Americans, including adolescents, to cope. Religion can be described as a personal or communal system of religious attitudes, practices and beliefs. Spirituality is generally described as the feelings, experiences, and practices that arise from the search for the sacred or God. We hypothesize that the experience of illness and BMT would affect what adolescents and young adults (A/YA) believe about R/S and their way of using faith to make meaning and to cope. The specific aim was to understand from the patients' perspective how they use R/S and how their R/S changes in the course of their BMT experience. Our goal is to develop a conceptual model of how R/S constructs operate in the experiences of A/YA undergoing BMT and also begin to develop an empirically-based pastoral care intervention. This is a qualitative study of R/S in persons aged 13-29 years undergoing HSCT or BMT. Semi-structured interviews are completed in the first 100 days post-transplant and at 1- year post-transplant. Interviews are audiotaped, transcribed, and coded for common themes using grounded theory methodology. Seven interviews (50% of those eligible) have been completed. Preliminary analysis shows that prayer is the most commonly used R/S practice, and that the majority of participants believe that their illnesses are "part of God's plan". Without the development of evidence for clinical practice, chaplains may offer care which may or may not be effective. We will propose a conceptual model suitable for future testing, and ultimately contribute to a better psycho- social- and spiritual- outcomes for A/YA undergoing BMT or HSCT.

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DRUG INTERACTION BETWEEN ORAL VORICONAZOLE AND ORAL CALCINEURIN INHIBITOR AND ITS RELATIONSHIP WITH BLOOD CONCENTRATION OF VORICONAZOLE IN RECIPIENTS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Drug interaction between calcineurin inhibitors (cyclosporine A (CsA) and tacrolimus) and voriconazole is well known. However, it has yet to be fully evaluated in the setting of hematopoietic stem cell transplantation (HSCT). We have previously shown a wide variability in the drug interaction between voriconazole and calcineurin inhibitors in HSCT recipients, which led to a conclusion that uniform reduction of the dose of calcineurin inhibitors was not recommended on initiating voriconazole. However, in that study, the route of administration of both drugs was not taken into consideration. In the present study, the magnitude of drug interaction between oral voriconazole and oral CsA was examined in HSCT recipients, and its relation with the blood concentration of voriconazole was also evaluated.
Patients and Methods: Nineteen recipients of allogeneic HSCT who had already been on a steady dose of oral CsA, and were started on oral voriconazole (200 mg per body every 12 h) for the treatment or prophylaxis of fungal infection could be evaluated. The concentration/dose (C/D; (ng/ml)/(mg/kg)) ratio of CsA was calculated 7–10 days after initiating voriconazole when the increased blood levels of calcineurin inhibitors had stabilized. The plasma level of voriconazole was measure by high-performance liquid chromatography.
Results: The median C/D ratio of CsA significantly increased to 113.7 (ng/ml)/(mg/kg) (range, 62.4-189.5) after initiating voriconazole administration as compared with that before (63.1 (range, 41.1-189.0): $P<0.001$). Median increased rate of C/D ratios were 83.0% with a range of 0.3% to 224.7%. The plasma level of voriconazole on the day of evaluating C/D ratio was 1.98±0.84 mg/ml. The increased rate of C/D ratio of tacrolimus did not correlate with the plasma level of voriconazole (r = -0.17, P = 0.50).
Conclusion: The magnitude of the drug interaction between oral CsA and oral voriconazole demonstrates a wide variability, whose increased rate of C/D ratio ranged between 0.3% and over 200%. This wide variability could not be explained by the bioavailability of voriconazole. The mechanisms of this variability should be explored in a future study.